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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	G. Duke Virca, Timothy A. Bird, Dirk M. Anderson, and John S. Marken	Docket No.:	2877-USA
Serial No.:	- not yet assigned - (Divisional of 09/509,902)		
Filing Date:	December 18, 2001		
For:	METHODS OF SCREENING FOR ANTAGONISTS AND AGONISTS OF POLYPEPTIDES HAVING KINASE FUNCTIONS		

BOX PATENT APPLICATION
Assistant Commissioner for Patents
Washington, DC 20231

REMARKS

This application is filed with a new, clean copy of the specification that incorporates amendments as described below.

Amendments Entered During Prosecution of the Prior Application (09/509,902):

In the Specification:

Paragraph at page 1, lines 7-10 deleted and replaced (December 1, 2000).

In the Claims:

Claims 1-36 canceled and new claims 37-55 added (April 3, 2000).

Claims 39 and 40 canceled, claims 37-38, 41-43, and 47-49 amended, and new claims 56-70 added (December 1, 2000).

Claims 45-46 and 50-55 canceled (December 11, 2000).

Result: Claims 37-38, 41-44, 47-49, and 56-70 pending in 09/509,902.

In the Sequence Listing:

Replaced in its entirety (December 1, 2000).

Additional New Amendments:

In the Title:

The Title, appearing at page 1, line 1 of the specification, has been deleted in its entirety and replaced with the following:

METHODS OF SCREENING FOR ANTAGONISTS AND AGONISTS OF POLYPEPTIDES HAVING KINASE FUNCTIONS

In the Specification:

At page 1, the paragraph at lines 7-11 (entitled "CROSS-REFERENCE TO RELATED APPLICATIONS") has been deleted in its entirety and replaced with the following paragraph:

This application is a divisional of U.S. Serial No. 09/509,902, having a filing date under 35 U.S.C. § 102 (e) of June 23, 2000; which is a national application under 35 U.S.C. § 371 of International Application No. PCT/US99/17630, having an international filing date of 03 August 1999 and published in English on February 17, 2000; which claims the priority of provisional applications U.S. Serial No. 60/095,270, filed 04 August 1998, and U.S. Serial No. 60/099,972, filed 11 September 1998; all of which are incorporated by reference herein.

In the Claims

Claims 37-38, 41-44, 47-49, and 56-70 (pending in prior application 09/509,902) have been canceled and replaced with the following new claims 71-100:

71 (NEW). A method of screening a candidate molecule to identify its ability to inhibit (antagonize) or agonize a recombinant polypeptide encoded by a nucleic acid molecule comprising the sequence of SEQ ID NO:5 or of SEQ ID NO:13, said method comprising the steps of:

(a) adding the candidate molecule to a medium which contains the polypeptide;

(b) determining the level of a biological activity in the medium; and

(c) comparing the level of biological activity of step (b) with the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule;

wherein a decreased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule, indicates an antagonist; and an increased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule, indicates an agonist.

72 (NEW). The method of claim 71 wherein the nucleic acid molecule encodes an amino acid sequence comprising the sequence of SEQ ID NO:11, or of SEQ ID NO:14, or of Leu-2 through Val-505 of SEQ ID NO:11.

73 (NEW). The method of claim 71 wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:11, or of SEQ ID NO:14, or of Leu-2 through Val-505 of SEQ ID NO:11.

74 (NEW). The method of claim 71 wherein the recombinant polypeptide is a purified polypeptide.

75 (NEW). The method of claim 71 wherein the recombinant polypeptide is produced by cells in the medium.

76 (NEW). The method of claim 75 wherein the recombinant polypeptide is produced according to a method comprising culturing a recombinant host cell comprising a nucleic acid molecule comprising the sequence of SEQ ID NO:5 or of SEQ ID NO:13 under conditions promoting expression of said polypeptide.

77 (NEW). The method of claim 76, wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, plant cells, insect cells, and animal cells.

78 (NEW). The method of claim 71 wherein the medium comprises a substrate of the polypeptide.

79 (NEW). The method of claim 78 wherein the substrate comprises a recognition motif comprising a serine, a threonine, and/or a tyrosine residue.

80 (NEW). The method of claim 71 wherein the biological activity is selected from the group consisting of phosphorylation of a substrate of the polypeptide, cell proliferation, and apoptotic cell death.

81 (NEW). The method of claim 71 wherein the medium comprises ^{32}P.

82 (NEW). The method of claim 71 wherein the method is used to identify antagonists and agonists from cells, cell-free preparations, chemical libraries, or natural product mixtures.

83 (NEW). The method of claim 71 wherein the candidate molecule is selected from the group consisting of natural or modified enzymes; natural or modified substrates, ligands, or receptors of the polypeptide; structural or functional mimetics of the polypeptide; catalytically inactive mutants of the polypeptide; small molecules; peptides; antibodies that bind to the polypeptide; and antisense molecules capable of blocking transcription or translation of mRNA encoding the polypeptide.

84 (NEW). A method of screening a candidate molecule to identify its ability to inhibit (antagonize) or agonize a recombinant polypeptide encoded by a nucleic acid molecule comprising the sequence of SEQ ID NO:6 or of SEQ ID NO:15, said method comprising the steps of:

(a) adding the candidate molecule to a medium which contains the polypeptide;

(b) determining the level of a biological activity in the medium; and

(c) comparing the level of biological activity of step (b) with the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule;

wherein a decreased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule, indicates an antagonist; and an increased level of biological activity of step (b), as compared to the level of biological activity that occurs in the

medium in the presence of the polypeptide and the absence of the candidate molecule, indicates an agonist.

85 (NEW). The method of claim 84 wherein the nucleic acid molecule encodes an amino acid sequence comprising the sequence of SEQ ID NO:12 or of Pro-2 through Glu-499 of SEQ ID NO:12.

86 (NEW). The method of claim 84 wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:12 or of Pro-2 through Glu-499 of SEQ ID NO:12.

87 (NEW). The method of claim 84 wherein the recombinant polypeptide is a purified polypeptide.

88 (NEW). The method of claim 84 wherein the recombinant polypeptide is produced by cells in the medium.

89 (NEW). The method of claim 88 wherein the recombinant polypeptide is produced according to a method comprising culturing a recombinant host cell comprising a nucleic acid molecule comprising the sequence of SEQ ID NO:6 or of SEQ ID NO:15 under conditions promoting expression of said polypeptide.

90 (NEW). The method of claim 89, wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, plant cells, insect cells, and animal cells.

91 (NEW). The method of claim 84 wherein the medium comprises a substrate of the polypeptide.

92 (NEW). The method of claim 91 wherein the substrate comprises a recognition motif comprising a serine, a threonine, and/or a tyrosine residue.

93 (NEW). The method of claim 84 wherein the biological activity is selected from the group consisting of phosphorylation of a substrate of the polypeptide, cell proliferation, and apoptotic cell death.

94 (NEW). The method of claim 84 wherein the medium comprises ^{32}P.

95 (NEW). The method of claim 84 wherein the method is used to identify antagonists and agonists from cells, cell-free preparations, chemical libraries, or natural product mixtures.

96 (NEW). The method of claim 84 wherein the candidate molecule is selected from the group consisting of natural or modified enzymes; natural or modified substrates, ligands, or receptors of the polypeptide; structural or functional mimetics of the polypeptide; catalytically inactive mutants of the polypeptide; small molecules; peptides; antibodies that bind to the polypeptide; and antisense molecules capable of blocking transcription or translation of mRNA encoding the polypeptide.

97 (NEW). A method of screening a candidate molecule to identify its ability to inhibit (antagonize) or agonize a recombinant polypeptide comprising the amino acid sequence of Pro-2 through Glu-499 of SEQ ID NO:12, said method comprising the steps of:

(a) adding the candidate molecule to a medium which contains the polypeptide and a substrate of the polypeptide;

(b) determining the level of a biological activity in the medium; and

(c) comparing the level of biological activity of step (b) with the level of biological activity that occurs in the medium in the presence of the polypeptide and the substrate and the absence of the candidate molecule;

wherein a decreased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the substrate and the absence of the candidate molecule, indicates an antagonist; and an increased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the substrate and the absence of the candidate molecule, indicates an agonist.

98 (NEW). The method of claim 97 wherein the recombinant polypeptide is a purified polypeptide.

99 (NEW). The method of claim 97 wherein the recombinant polypeptide is produced by cells in the medium.

100 (NEW). The method of claim 97 wherein the substrate comprises a recognition motif comprising a serine and/or a threonine residue.

These amendments to the claims are supported by the claims as filed in the prior application 09/509,902, by the specification generally and, in particular, by the following portions of the specification:

page 5, lines 26-27;
page 8, line 30 through page 10, line 13;
page 11, line 30 through page 13, line 16;
page 14, lines 16-18;
page 16, lines 12-13;
page 22, lines 13-29;
page 26, lines 14-18;
page 29, lines 26-29;
page 32, lines 5-8;
page 34, lines 9-22;
page 35, lines 27-32;
page 36, lines 1-14 and 23-25;
page 38, lines 5-15; and
page 42, line 11 through page 43, line 22.

No new matter has been added.

For the convenience of the Examiner an Appendix presenting marked-up versions of the specification and claims, as amended, is appended.

Information Disclosure Statement

Also submitted herewith is an Information Disclosure Statement and a Form PTO-1449.

If a telephone interview would be helpful in advancing the prosecution of this application, Applicants' attorney invites the Examiner to contact her at the number provided below.

Respectfully submitted,

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APPENDIX
U.S. Serial No. - not yet assigned - (Divisional of 09/509,902)
Claims Under Consideration (New Claims 71-100)
Version with markings to show changes made

In the Title:

The Title, appearing at page 1, lines 1-2 of the specification:

METHODS OF SCREENING FOR ANTAGONISTS AND AGONISTS OF[HUMAN cDNAs ENCODING] POLYPEPTIDES HAVING KINASE FUNCTIONS

In the Specification:

At page 1, the paragraph at lines 7-13 (entitled "CROSS-REFERENCE TO RELATED APPLICATIONS"):

This application is a divisional of U.S. Serial No. 09/509,902, having a filing date under 35 U.S.C. § 102 (e) of June 23, 2000; which is a national application under 35 U.S.C. § 371 of International Application No. PCT/US99/17630, having an international filing date of 03 August 1999 and published in English on February 17, 2000; which claims the priority of provisional applications U.S. Serial No. 60/095,270, filed 04 August 1998, and U.S. Serial No. 60/099,972, filed 11 September 1998; all of which are incorporated by reference herein.

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71 (NEW). A method of screening a candidate molecule to identify its ability to inhibit (antagonize) or agonize a recombinant polypeptide encoded by a nucleic acid molecule comprising the sequence of SEQ ID NO:5 or of SEQ ID NO:13, said method comprising the steps of:

(a) adding the candidate molecule to a medium which contains the polypeptide;

(b) determining the level of a biological activity in the medium; and

(c) comparing the level of biological activity of step (b) with the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule;

wherein a decreased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule, indicates an antagonist; and an increased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule, indicates an agonist.

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74 (NEW). The method of claim 71 wherein the recombinant polypeptide is a purified polypeptide.

75 (NEW). The method of claim 71 wherein the recombinant polypeptide is produced by cells in the medium.

76 (NEW). The method of claim 75 wherein the recombinant polypeptide is produced according to a method comprising culturing a recombinant host cell comprising a nucleic acid molecule comprising the sequence of SEQ ID NO:5 or of SEQ ID NO:13 under conditions promoting expression of said polypeptide.

77 (NEW). The method of claim 76, wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, plant cells, insect cells, and animal cells.

78 (NEW). The method of claim 71 wherein the medium comprises a substrate of the polypeptide.

79 (NEW). The method of claim 78 wherein the substrate comprises a recognition motif comprising a serine, a threonine, and/or a tyrosine residue.

80 (NEW). The method of claim 71 wherein the biological activity is selected from the group consisting of phosphorylation of a substrate of the polypeptide, cell proliferation, and apoptotic cell death.

81 (NEW). The method of claim 71 wherein the medium comprises ^{32}P.

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84 (NEW). A method of screening a candidate molecule to identify its ability to inhibit (antagonize) or agonize a recombinant polypeptide encoded by a nucleic acid molecule comprising the sequence of SEQ ID NO:6 or of SEQ ID NO:15, said method comprising the steps of:

(a) adding the candidate molecule to a medium which contains the polypeptide;

(b) determining the level of a biological activity in the medium; and

(c) comparing the level of biological activity of step (b) with the level of biological activity that occurs in the medium in the presence of the polypeptide and the absence of the candidate molecule;

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wherein a decreased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the substrate and the absence of the candidate molecule, indicates an antagonist; and an increased level of biological activity of step (b), as compared to the level of biological activity that occurs in the medium in the presence of the polypeptide and the substrate and the absence of the candidate molecule, indicates an agonist.

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